10084676

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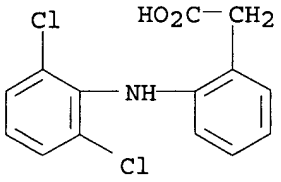
(FILE 'HOME' ENTERED AT 10:57:02 ON 02 JAN 2003)

FILE 'REGISTRY' ENTERED AT 10:57:11 ON 02 JAN 2003
L1 0 S DICLOPHENAC/CN
L2 1 S DICLOPHENAC
L3 1 S DICLOFENAC/CN

=> d l3

L3 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2003 ACS
RN 15307-86-5 REGISTRY
CN Benzeneacetic acid, 2-[(2,6-dichlorophenyl)amino]- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Acetic acid, [o-(2,6-dichloroanilino)phenyl]- (8CI)
OTHER NAMES:
CN 2-(2,6-Dichloroanilino)phenylacetic acid
CN 2-(2,6-Dichlorophenylamino)phenylacetic acid
CN 2-[(2,6-Dichlorophenyl)amino]benzeneacetic acid
CN Dichlofenac
CN **Diclofenac**
CN Diclofenac acid
CN Dicloreuma
CN N-(2,6-Dichlorophenyl)-o-aminophenylacetic acid
CN Pennsaid
CN Transfenac
CN [o-(2,6-Dichloroanilino)phenyl]acetic acid
DR 76595-40-9, 87180-41-4
MF C14 H11 Cl2 N O2
CI COM
LC STN Files: ADISINSIGHT, ADISNEWS, AGRICOLA, ANABSTR, BEILSTEIN*, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CANCERLIT, CAPLUS, CASREACT, CBNB, CEN, CHEMCATS, CHEMLIST, CIN, CSCHEM, CSNB, DDFU, DIOGENES, DRUGPAT, DRUGU, EMBASE, IFICDB, IFIPAT, IFIUDB, IPA, MEDLINE, MRCK*, PHAR, PHARMASEARCH, PROMT, RTECS*, SPECINFO, TOXCENTER, ULIDAT, USAN, USPAT2, USPATFULL, VETU
(*File contains numerically searchable property data)
Other Sources: EINECS**, WHO
(**Enter CHEMLIST File for up-to-date regulatory information)



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

2646 REFERENCES IN FILE CA (1962 TO DATE)
94 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
2654 REFERENCES IN FILE CAPLUS (1962 TO DATE)

blessing

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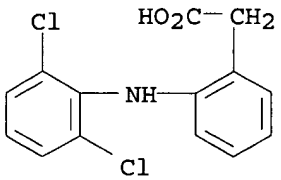
=> d l2

L2 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2003 ACS
RN 15307-79-6 REGISTRY
CN Benzeneacetic acid, 2-[(2,6-dichlorophenyl)amino]-, monosodium salt (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Acetic acid, [o-(2,6-dichloroanilino)phenyl]-, monosodium salt (8CI)
OTHER NAMES:
CN 2-(2,6-Dichloroanilino)phenylacetic acid sodium salt
CN Diclofen SR 100
CN Diclofenac sodium
CN Diclofenac sodium salt
CN **Diclophenac sodium**
CN Diklovit
CN Feloran
CN GP 45840
CN Hyanalgese D
CN Inflaban
CN N-(2,6-Dichlorophenyl)-o-aminophenylacetic acid sodium salt
CN Naclof
CN Orthofen
CN Orthophen
CN Sodium diclofenac
CN Sodium [o-(2,6-dichloroanilino)phenyl]acetate
CN Sorelmon
CN SR 318B
CN Voltaren
CN Voltaren Ophtha
CN Voltaren Ophtha CD
CN Voltarol
CN [o-(2,6-Dichloroanilino)phenyl]acetic acid sodium salt
MF C14 H11 Cl2 N O2 . Na
CI COM
LC STN Files: ADISINSIGHT, ADISNEWS, AGRICOLA, ANABSTR, BEILSTEIN*, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CAPLUS, CASREACT, CBNB, CEN, CHEMCATS, CHEMLIST, CIN, CSCHEM, DDFU, DIOGENES, DRUGPAT, DRUGU, EMBASE, IFICDB, IFIPAT, IFIUDB, IPA, MEDLINE, MRCK*, MSDS-OHS, NIOSHTIC, PHAR, PHARMASEARCH, PIRA, PROMT, RTECS*, TOXCENTER, ULIDAT, USAN, USPAT2, USPATFULL
(*File contains numerically searchable property data)
Other Sources: DSL**, EINECS**
(**Enter CHEMLIST File for up-to-date regulatory information)
CRN (15307-86-5)



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PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1614 REFERENCES IN FILE CA (1962 TO DATE)
17 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
1619 REFERENCES IN FILE CAPLUS (1962 TO DATE)

blessing

L3: Entry 101 of 179 File: USPT Sep 25, 2001

DOCUMENT-IDENTIFIER: US 6294195 B1
TITLE: Orally administrable opioid formulations having extended duration of effect

Detailed Description Text (2):
The multiparticulate systems of the present invention may incorporate one or more compounds known as opioid analgesics. Opioid analgesic compounds which may be used in the present invention include alfentanil, allylprodine, alphaprodine, anileridine, benzylmorphine, bezitramide, buprenorphine, butorphanol, clonitazene, codeine, cyclazocine, desomorphine, dextromoramide, dezocine, diampromide, dihydrocodeine, dihydromorphine, dimenoxadol, dimepheptanol, dimethylthiambutene, dioxaphetyl butyrate, dipipanone, eptazocine, ethoheptazine, ethylmethylthiambutene, ethylmorphine, etonitazene fentanyl, heroin, hydrocodone, hydromorphone, hydroxypethidine, isomethadone, ketobemidone, levallorphan, levorphanol, levophenacylmorphan, lofentanil, meperidine, meptazinol, metazocine, methadone, metopon, morphine, myrophine, nalbuphine, narceine, nicomorphine, norlevorphanol, normethadone, nalorphine, normorphine, norpipanone, opium, oxycodone, oxymorphone, papaveretum, pentazocine, phenadoxone, phenomorphan, phenazocine, phenoperidine, piminodine, piritramide, propheptazine, promedol, properidine, propiram, propoxyphene, sufentanil, tramadol, tilidine, salts thereof, mixtures of any of the foregoing, mixed mu-agonists/antagonists, mu-antagonist combinations, and the like.

Detailed Description Text (7):
The substrates of the present invention may further include one or more additional drugs which may or may not act synergistically with the opioid analgesics of the present invention. Examples of such additional drugs include non-steroidal anti-inflammatory agents, including ibuprofen, diclofenac, naproxen, benoxaprofen, flurbiprofen, fenoprofen, flubufen, ketoprofen, indoprofen, piroprofen, carprofen, oxaprozin, pramoprofen, muroprofen, trioxaprofen, suprofen, aminoprofen, tiaprofenic acid, fluprofen, bucloxic acid, indomethacin, sulindac, tolmetin, zomepirac, tiopinac, zidometacin, acemetacin, fentiazac, clidanac, oxpinac, mefenamic acid, meclofenamic acid, flufenamic acid, niflumic acid tolfenamic acid, diflurisal, flufenisal, piroxicam, sudoxicam or isoxicam, and the like. Other suitable additional drugs which may be included in the dosage forms of the present invention include acetaminophen, aspirin, and other non-opioid analgesics.

Other Reference Publication (17):
Abraham Sunshine, et al., "Analgesic oral efficacy of tramadol hydrochloride in postoperative pain", Clin. Pharmacol. Ther., Jun. 1992, pp. 740-746.

CLAIMS:

5. The dosage form of claim 1, wherein said opioid analgesic is selected form the group consisting of morphine, codeine, hydromorphone, hydrocodone, oxycodone, oxymorphone, dihydrocodeine, dihydromorphine, tramadol, and mixtures thereof.

6. The dosage form of claim 1, wherein said opioid analgesic is selected from the group consisting of alfentanil, allylprodine, alphaprodine, anileridine, benzylmorphine, bezitramide, buprenorphine, butorphanol, clonitazene, codeine, cyclazocine, desomorphine, dextromoramide, dezocine, diampromide, dihydrocodeine, dihydromorphine, dimenoxadol, dimepheptanol, dimethylthiambutene, dioxaphetyl butyrate, dipipanone, eptazocine, ethoheptazine, ethylmethylthiambutene, ethylmorphine, etonitazene fentanyl, heroin, hydrocodone, hydromorphone, hydroxypethidine, isomethadone, ketobemidone, levallorphan, levorphanol, levophenacyl morphan, lofentanil, meperidine, meptazinol, metazocine, methadone, metopon, morphine, myrophine, nalbuphine, narceine, nicomorphine, norlevorphanol, normethadone, nalorphine, normorphine, norpipanone,

opium, oxycodone, oxymorphone, papaveretum, pentazocine, phenadoxone, phenomorphan, phenazocine, phenoperidine, piminodine, piritramide, propheptazine, promedol, properidine, propiram, propoxyphene, sufentanil, tramadol, tilidine, salts thereof and mixtures thereof.

16. A bioavailable sustained-release oral analgesic dosage form for once-a-day administration, comprising:

a unit dose comprising a plurality of pharmaceutically acceptable matrices comprising an analgesically effective amount of tramadol or a salt thereof, ethylcellulose and stearyl alcohol, each of said matrices having a diameter from about 0.1 mm to about 3 mm, said dosage form being bioavailable and providing a therapeutic effect for about 24 hours or more after oral administration to a human patient.

20. The dosage form of claim 19, wherein said non-steroidal anti-inflammatory agent is selected from the group consisting of ibuprofen, diclofenac, naproxen, benoxaprofen, flurbiprofen, fenoprofen, flubufen, ketoprofen, indoprofen, piroprofen, carprofen, oxaprozin, pramoprofen, muroprofen, trioxaprofen, suprofen, aminoprofen, tiaprofenic acid, fluprofen, bucloxic acid, indomethacin, sulindac, tolmetin, zomepirac, tiopinac, zidometacin, acemetacin, fentiazac, clidanac, oxpinac, mefenamic acid, meclofenamic acid, flufenamic acid, niflumic acid tolfenamic acid, diflurisal, flufenisal, piroxicam, sudoxicam or isoxicam, and mixtures of any of the foregoing.

21. The dosage form of claim 1, wherein said opioid analgesic consists of tramadol or a salt thereof.

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L3: Entry 101 of 179 File: USPT Sep 25, 2001

US-PAT-NO: 6294195
DOCUMENT-IDENTIFIER: US 6294195 B1

TITLE: Orally administrable opioid formulations having extended duration of effect

DATE-ISSUED: September 25, 2001

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Oshlack; Benjamin	New York	NY		
Chasin; Mark	Manalapan	NJ		

US-CL-CURRENT: 424/457; 424/456, 424/484, 424/486, 424/487, 424/488, 424/489, 514/772.3, 514/781, 514/951

CLAIMS:

What is claimed is:

1. A bioavailable sustained-release oral analgesic dosage form for once-a-day administration, comprising:

a unit dose comprising an analgesically effective amount of a plurality of pharmaceutically acceptable matrices comprising an opioid analgesic or a salt thereof, and a hydrophobic material selected from the group consisting of an alkylcellulose, an acrylic resin and mixtures thereof, said matrices further comprising at least one C.sub.12 to C.sub.36 aliphatic alcohol, each of said matrices having a diameter from about 0.1 mm to about 3 mm, said dosage form being bioavailable and providing a therapeutic effect for about 24 hours or more after oral administration to a human patient.

2. A bioavailable sustained-release oral analgesic dosage form for once-a-day administration, comprising:

a unit dose comprising a plurality of pharmaceutically acceptable matrices comprising an analgesically effective amount of hydromorphone or a salt thereof, ethylcellulose and stearyl alcohol, each of said matrices having a diameter from about 0.1 mm to about 3 mm, said dosage form being bioavailable and providing a therapeutic effect for about 24 hours or more after oral administration to a human patient.

3. The dosage form of claim 1, wherein said matrices further comprise at least one polyalkylene glycol.

4. The dosage form of claim 1, wherein said C.sub.12 to C.sub.36 aliphatic alcohol is stearyl alcohol.

5. The dosage form of claim 1, wherein said opioid analgesic is selected form the group consisting of morphine, codeine, hydromorphone, hydrocodone, oxycodone, oxymorphone, dihydrocodeine, dihydromorphine, tramadol, and mixtures thereof.

6. The dosage form of claim 1, wherein said opioid analgesic is selected from the group consisting of alfentanil, allylprodine, alphaprodine, anileridine, benzylmorphine, bezitramide, buprenorphine, butorphanol, clonitazene, codeine, cyclazocine, desomorphine, dextromoramide, dezocine, diampromide, dihydrocodeine, dihydromorphine, dimenoxadol, dimepheptanol, dimethylthiambutene, dioxaphetyl butyrate, dipipanone, eptazocine, ethoheptazine, ethylmethylthiambutene, ethylmorphine, etonitazene fentanyl, heroin, hydrocodone, hydromorphone, hydroxypethidine, isomethadone, ketobemidone, levallorphan, levorphanol, levophenacyl morphan, lofentanil, meperidine, meptazinol, metazocine, methadone, metopon, morphine, myrophine, nalbuphine, narceine, nicomorphine, norlevorphanol, normethadone, nalorphine, normorphine, norpipanone, opium, oxycodone, oxymorphone, papaveretum, pentazocine, phenadoxone, phenomorphan, phenazocine, phenoperidine, piminodine, piritramide, propheptazine, promedol, properidine, propiram, propoxyphene, sufentanil, tramadol, tilidine, salts thereof and mixtures thereof.

7. The dosage form of claim 5, wherein said opioid analgesic consists of from about 2 mg to about 64 mg hydromorphone.

8. The dosage form of claim 5, wherein said opioid analgesic consists of from about 5 mg to about 800 mg morphine.

9. The dosage form of claim 1, wherein said opioid analgesic consists of from about 5 mg to about 400 mg oxycodone.

10. The dosage form of claim 1 which provides a peak plasma level of said opioid in-vivo from about 2 to about 10 hours after administration.

11. The dosage form of claim 1 which provides a peak plasma level of said opioid in-vivo from about 2 to about 4 hours after administration.

12. The dosage form of claim 1, wherein said matrices further comprise a hydroxyalklcellulose selected from the group consisting of hydroxypropylcellulose, hydroxypropylmethylcellulose, hydroxyethylcellulose and mixtures of any of the foregoing.

13. The dosage form of claim 12, wherein said hydroxyalkylcellulose is hydroxyethylcellulose.

14. The dosage form of claim 1, wherein said unit dose of said matrices are contained within a hard gelatin capsule.

15. The dosage form of claim 1, wherein said matrices have a diameter from about 0.5 mm to about 2 mm.

16. A bioavailable sustained-release oral analgesic dosage form for once-a-day administration, comprising:

a unit dose comprising a plurality of pharmaceutically acceptable matrices comprising an analgesically effective amount of tramadol or a salt thereof, ethylcellulose and stearyl alcohol, each of said matrices having a diameter from about 0.1 mm to about 3 mm, said dosage form being bioavailable and providing a therapeutic effect for about 24 hours or more after oral administration to a human patient.

17. The dosage form of claim 1, further comprising release-modifying agents, said release-modifying agents comprising one or more hydrophilic polymers.

18. A dosage form of claim 1, further comprising a non-opioid drug.

19. The dosage form of claim 18, wherein the said non-opioid drug is a non-steroidal anti-inflammatory agent.

20. The dosage form of claim 19, wherein said non-steroidal anti-inflammatory agent is selected from the group consisting of ibuprofen, diclofenac, naproxen, benoxaprofen, flurbiprofen, fenoprofen, flubufen, ketoprofen, indoprofen, piroprofen, carprofen, oxaprozin, pramoprofen, muroprofen, trioxaprofen, suprofen, aminoprofen, tiaprofenic acid, fluprofen, bucloxic acid, indomethacin, sulindac, tolmetin, zomepirac, tiopinac, zidometacin, acemetacin, fentiazac, clidanac, oxpinac, mefenamic acid, meclofenamic acid, flufenamic acid, niflumic acid tolfenamic acid, diflurisal, flufenisal, piroxicam, sudoxicam or isoxicam, and mixtures of any of the foregoing.

21. The dosage form of claim 1, wherein said opioid analgesic consists of tramadol or a salt thereof.

22. The dosage form of claim 1, wherein said alkylcellulose is ethylcellulose.

23. The dosage form of claim 2 which provides a peak plasma level of said opioid in-vivo from about 2 to about 10 hours after administration to a patient or a population of patients.

24. The dosage form of claim 2 which provides a peak plasma level of said opioid in-vivo from about 2 to about 4 hours after administration to a patient or a population of patients.

25. The dosage form of claim 16 which provides a peak plasma level of said opioid in-vivo from about 2 to about 10 hours after administration to a patient or a population of patients.

26. The dosage form of claim 16 which provides a peak plasma level of said opioid in-vivo from about 2 to about 4 hours after administration to a patient or a population of patients.

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L3: Entry 89 of 179 File: USPT Aug 20, 2002

US-PAT-NO: 6436438
DOCUMENT-IDENTIFIER: US 6436438 B1

TITLE: Tramadol multiple unit formulations

DATE-ISSUED: August 20, 2002

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Momberger; Helmut	Marburg			DE
Raber; Marc	Giessen			DE
Kuhn; Dieter	Marburg			DE
Schmid; Wolfgang	Lohra			DE

ASSIGNEE-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY	TYPE CODE
Asto-Medica AG	Radebeul			DE	03

APPL-NO: 09/ 349564 [PALM]
DATE FILED: July 8, 1999

PARENT-CASE:
This application is a Divisional of Ser. No. 08/896,629 filed Jul. 18, 1997 now U.S. Pat. No. 5,955,104.

FOREIGN-APPL-PRIORITY-DATA:

COUNTRY	APPL-NO	APPL-DATE
DE	196 30 035	July 25, 1996

INT-CL: [07] A61 K 9/22, A61 K 9/54, A61 K 9/60, A61 K 9/62

US-CL-ISSUED: 424/458; 424/457, 424/459, 424/461, 424/462, 424/468, 424/494, 424/495, 424/496, 424/497, 514/770, 514/781, 514/782, 514/951
US-CL-CURRENT: 424/458; 424/457, 424/459, 424/461, 424/462, 424/468, 424/494, 424/495, 424/496, 424/497, 514/770, 514/781, 514/782, 514/951

FIELD-OF-SEARCH: 424/472, 424/458, 424/459, 424/461, 424/462, 424/494, 424/495, 424/497, 424/457, 424/468, 424/496, 424/456, 424/469, 424/470

PRIOR-ART-DISCLOSED:

U.S. PATENT DOCUMENTS

Search Selected Search ALL

	PAT-NO	ISSUE-DATE	PATENTEE-NAME	US-CL
☐	5026560	June 1991	Makino et al.	424/494
☐	5344657	September 1994	Desmolin	424/458
☐	5478577	December 1995	Sackler et al.	424/489
☐	5567441	October 1996	Chen	424/494
☐	5955104	September 1999	Momberger et al.	424/458

ART-UNIT: 1615

PRIMARY-EXAMINER: Spear; James M.

ABSTRACT:

A multiple unit oral pharmaceutical dosage form having a plurality of pellets in a water soluble capsule or in a tablet compressed from the pellets, wherein each pellet contains (a) a substantially inert core, (b) an active ingredient layer over the inert core, and containing (i) a pharmacologically active particulate active ingredient, (ii) a nonembedding amount of a binder for adhering the active ingredient over the inert core, and optionally (iii) a pharmaceutically acceptable, inert adjuvant, such as colloidal silica, and (c) a coating over the active ingredient layer for retarding the release of the active ingredient from the active ingredient layer into an aqueous body fluid solvent in situ, the nonembedding amount of the binder is suitably from about 1% wt. to about 10% wt. based on the active ingredient layer, the binder in the active ingredient layer is suitably a mixture of ethylcellulose and shellac, in a weight proportion suitably of from about 1: about 9, to from about 9: about 1, the coating for retarding the release suitably contains from about 70% wt. to about 95% wt. based on the coating, of a substantially water-insoluble, pharmacologically inert, particulate material, and a binder; the pharmacologically inert, particulate material is suitably talcum, and the binder in the active ingredient layer is suitably identical to the binder in the coating.

20 Claims, 7 Drawing figures

L2: Entry 15 of 16 File: USPT Sep 22, 1998

DOCUMENT-IDENTIFIER: US 5811459 A
TITLE: Ortho substituted aromatic compounds useful as antagonists of the pain enhancing effects of E-type prostaglandins

Brief Summary Text (3):
Non-steroidal anti-inflammatory drugs (NSAIDS) and opiates are the main classes of drugs in pain relief. However both possess undesireable side effects. NSAIDS are known to cause gastrointestinal irritation and opiates are known to be addictive.

Brief Summary Text (4):
We have now found a class of compounds structurally different to NSAIDS and opiates, and useful in the relief of pain.

Brief Summary Text (201):
By virtue of their ability to relieve pain, the compounds of the formula I are of value in the treatment of certain inflammatory an non-inflammatory conditions which are currently treated with a cyclooxygenase-inhibitory non-steroidal anti- inflammatory drug (NSAID) such as indomethacin, ketorolac, acetylsalicyclic acid, ibuprofen, sulindac, tolmetin and piroxicam or other analgesics such as paracetamol, tramadol, Codein or in some circumstances morphine. Co-administration of a compound of the formula I with a NSAID can result in a reduction of the quantity of the latter agent needed to produce a therapeutic effect. Thereby the likelihood of adverse side-effects from the NSAID such as gastrointestinal effects are reduced. Thus according to a further feature of the invention there as provided a pharmaceutical composition which comprises a compound of the formula (I), or an in-vivo hydrolysable ester or amide or pharmaceutically-acceptable salt thereof, in conjunction or admixture with a cyclooxygenase inhibitory non-steroidal anti-inflammatory agent, and a pharmaceutically-acceptable diluent or carrier.

Detailed Description Text (30):
b:- (4-Carboxymethylphenylmethyl)triphenylphosphonium bromide prepared in the standard way from 4-(bromomethyl)phenylacetic acid and triphenylphosphine.

Detailed Description Paragraph Table (2):

##STR26##

Compd Foot- No. R1 Link R2 m.p. note

1 H CH.sub.2 CH.sub.2 CO.sub.2 H 143-144 a 2 H CH.sub.2 CH.sub.2 CH.sub.2 CO.sub.2 H 88-89 b 3 5-Cl CH.sub.2 CH.sub.2 CH.sub.2 CO.sub.2 H 91-92 b 4 5-F CH.sub.2 CH.sub.2 CH.sub.2 CO.sub.2 H 102-103 5 5-Cl CH.sub.2 CH.sub.2 CH.sub.2 CO.sub.2 H 95.5-96.5 6 5-OMe CH.sub.2 CH.sub.2 CH.sub.2 CO.sub.2 H 102-103 7 6-OMe CH.sub.2 CH.sub.2 CH.sub.2 CO.sub.2 H 90-91 8 4-OMe CH.sub.2 CH.sub.2 CH.sub.2 CO.sub.2 H 121-121.5 9 6-F CH.sub.2 CH.sub.2 CH.sub.2 CO.sub.2 H 92-93 10 3,5-diCl CH.sub.2 CH.sub.2 CH.sub.2 CO.sub.2 H 163-163.5 11 5-NO.sub.2 CH.sub.2 CH.sub.2 CH.sub.2 CO.sub.2 H 161-163 c 12 5-NH.sub.2 CH.sub.2 CH.sub.2 CH.sub.2 CO.sub.2 H 152-155 d 13 5-NHCOMe CH.sub.2 CH.sub.2 CH.sub.2 CO.sub.2 H 181-183 e 14 5-NHCO.sub.2 Et CH.sub.2 CH.sub.2 CH.sub.2 CO.sub.2 H 165-167 f 15 5-NHSO.sub.2 Ph CH.sub.2 CH.sub.2 CH.sub.2 CO.sub.2 H 159-161 g 16 5-NHMe CH.sub.2 CH.sub.2 CH.sub.2 CO.sub.2 H 153-154 h 17 5-NEt.sub.2 CH.sub.2 CH.sub.2 CH.sub.2 CO.sub.2 H 67-68 i 18 5-COMe CH.sub.2 CH.sub.2 CH.sub.2 CO.sub.2 H 147-147.5 j 19 5-CO-nPentyl CH.sub.2 CH.sub.2 CH.sub.2 CO.sub.2 H 136-136.5 k 20 5-n-Hexyl CH.sub.2 CH.sub.2 CH.sub.2 CO.sub.2 H 91.5-92 l 21 5-Br CH.sub.2 CH.sub.2 CH.sub.2 CO.sub.2 H 115-118 m 22 5-CN CH2CH2CH2 CO.sub.2 H 134-135 n 23 5-CHO CH.sub.2 CH.sub.2 CH CO.sub.2 H 126-127 o 24 5-CH.sub.2 OH CH.sub.2 CH.sub.2 CH.sub.2 CO.sub.2 H 102-103 p 25 5-C(NOH)Me CH.sub.2 CH.sub.2 CH.sub.2 CO.sub.2 H 166.5-167.5 q 26 5-C(NOH)H CH.sub.2 CH.sub.2 CH.sub.2 CO.sub.2 H 143.5-144 r 27 5-C(NOMe)Me CH.sub.2 CH.sub.2 CH.sub.2

CO.sub.2 H 121-122 s 28 5-Cl CH.sub.2 CH.sub.2 CO.sub.2 H 145-147 a 29 5-NO.sub.2 CH.sub.2 CH.sub.2 CO.sub.2 H 183-184 a,t 30 5-SOMe CH.sub.2 CH.sub.2 CH.sub.2 CO.sub.2 H 101-102 u 31 5-SO.sub.2 Me CH.sub.2 CH.sub.2 CH.sub.2 CO.sub.2 H 185 v 32 H CH.sub.2 CH.sub.2 CH.sub.2 CONHCH.sub.2 CO.sub.2 H 101-102 w 33 H CH.sub.2 CH.sub.2 CH.sub.2 CONH(CH.sub.2).sub.2 CO.sub.2 115-116 x 34 5,6-CHCHCHCH CH.sub.2 CH.sub.2 CH.sub.2 CO.sub.2 H 128-130 35 5,6-(CH.sub.2).sub.4 CH.sub.2 CH.sub.2 CH.sub.2 CO.sub.2 H 138-139 y 36 3-NO.sub.2 CH.sub.2 CH.sub.2 CH.sub.2 CO.sub.2 H 117-119 37 5-C(O)CHMe.sub.2 (CH.sub.2).sub.3 CO.sub.2 H 135-137 z 38 5-C(NOH)CHMe.sub.2 (CH.sub.2).sub.3 CO.sub.2 H 170-176 (aa) 39 5-COEt (CH.sub.2).sub.3 CO.sub.2 H 116-118 (ab) 40 5-COPh (CH.sub.2).sub.3 CO.sub.2 H 142-144 (ac) 41 5-C(NOH)Et (CH.sub.2).sub.3 CO.sub.2 H 168-170 (aa) 42 5-C(NOH)Ph (CH.sub.2).sub.3 CO.sub.2 H 180-189 (aa) 43 5-C(NNHCONH.sub.2)CH.sub.3 (CH.sub.2).sub.3 CO.sub.2 H 158-160 (ad) 44 5-C(NHNH.sub.2)CH.sub.3 (CH.sub.2).sub.3 CO.sub.2 H 174-180 (ae) 45 5-C(NHNHPh)CH.sub.3 (CH.sub.2).sub.3 CO.sub.2 H 143-147 (af) 46 5-CH.sub.2 OMe (CH.sub.2).sub.3 CO.sub.2 H 81-84 (ag) 47 5-CH.sub.2 SMe (CH.sub.2).sub.3 CO.sub.2 H 107.5-111 (ah) 48 5-CH.sub.2 SO.sub.2 Me (CH.sub.2).sub.3 CO.sub.2 H 159.5-164 (ai) 49 5-CH.sub.2 SOMe (CH.sub.2).sub.3 CO.sub.2 H 137.5-140.5 (ai) 50 ##STR27## (CH.sub.2).sub.3 CO.sub.2 H 177.5-181.5 (aj) 51 5-NEt.sub.2 (CH.sub.2).sub.3 CO.sub.2 H 67-68 (ak) 52 5-Br (CH.sub.2).sub.2 CO.sub.2 H 166-167 (al)

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a: (4-Carboxyphenylmethyl)triphenylphosphonium bromide was prepared in the standard way from 4-(bromomethyl)benzoic acid and triphenylphosphine. b: (4-Carboxymethylphenylmethyl)triphenylphosphonium bromide was prepared in the standard way from 4-(bromomethyl)phenylacetic acid and triphenylphosphine. c: Methyl 4-[3-(2-hydroxy-5-nitrophenyl)propyl]benzoate was prepared from methyl 4-[3-(2-hydroxyphenyl)propyl]benzoate (see Example 1) as follows: Nitric acid (15M, 3.13 ml) was added to acetic anhydride (12.52 ml) a 0.degree. C. and the mixture stirred for 15 minutes, then added to a stirred solution of methyl 4-[3-(2-hydroxy-phenyl)propyl]benzoate (12.89 g) in acetic anhydride (300 ml) at 0.degree. C. and stirred for 18 hours. The solvent was evaporated and the resulting yellow oil purified by chromatography on silica gel using ethyl acetate:hexane (1:9 to 1:1 gradient) as eluant to give methyl 4-[3-(2- hydroxy-3-nitrophenyl)propyl]benzoate (5.4 g) and methyl 4-[3-(2-hydroxy-5-nitro- phenyl)propyl]benzoate (7.5 g). d: Methyl 4-[3-(2-benzyloxy-5-aminophenyl)propyl]benzoate was prepared from methyl 4-[3-(2-benzyloxy-5-nitrophenyl)propyl]benzoate using the process described in Example 2, note a. e: Methyl 4-[3-(2-benzyloxy-5-methylcarbonylaminophenyl)propyl]benzoate was prepared from methyl 4-[3-(2-benzyloxy-5-aminophenyl)-propyl]benzoate by the method described in Example 2, note b.

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